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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/727,769	12/04/2000	Shotaro Yamaguchi	Q62106	5479

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EXAMINER	
RAO, MANJUNATH N	
ART.UNIT	PAPER NUMBER
1652	22

DATE MAILED: 05/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

Office Action Summary	Application No.	Applicant(s)	
	09/727,769	YAMAGUCHI, SHOTARO	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21 and 24-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *27,28,31,32,35 and 36* is/are allowed.

6)☒ Claim(s) *21,24-26,29,30,33,34 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 21, 24-37 are still at issue and are present for examination.

Applicants' amendments and arguments filed on 2-13-03, paper No.20, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26, 30, 34, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 26, 30, 34 recite the phrase " derived from ....*Chryseobacterium*". The metes and bounds of this phrase is not clear to the Examiner. While the term "derive" can mean "to isolate from or obtain from a source", the above term can also mean "to arrive at by reasoning i.e., to deduce or infer" or also "to produce or obtain from another substance". Therefore, it is not clear to the Examiner either from the specification or from the claims as to what applicants mean by the above phrase. It is not clear to the Examiner whether the phrase "derived from ....*Chryseobacterium*" encompasses a single specific polypeptide as in "isolated from *Chryseobacterium*" or whether it encompasses recombinants, variants and mutants of a *Chryseobacterium* polypeptide of any source and labeled as "derived from ....*Chryseobacterium*". As applicants have not provided a definition for the above phrase, Examiner has interpreted the claims broadly to mean, that polypeptides "derived from

....*Chryseobacterium*" encompasses polypeptide sequences with said activity but which are which are recombinants, variants, or mutants from any source. Examiner has given the same interpretation while considering the claims for all other rejections.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29, 33, and 37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 29, 33, and 37 recite the phrase "homology of 80% or more". Claims 29, 33, and 37 are drawn to a method for improving the functionality of food or modifying a protein or peptide by using an enzyme encoded by a polynucleotide which has a homology of "80% or more" with polynucleotides claimed in parts (a) and (b) of respective claims. However, a perusal of the specification indicates that applicants have no support for the phrase "homology of 80% or more". Thus said phrase constitutes "new matter". Therefore claims 29, 33, and 37 are rejected for introducing "new matter" into the claims.

Claims 21, 24-26, 29-30, 33, 34, 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of deamidating amido groups in protein or peptides in a food using the deamidating enzyme with SEQ ID NO:6, does not reasonably provide enablement for such a method using any such deamidating enzyme from any

source. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 21, 24-26, 29-30, 33, 34, 37 are specifically drawn to a method of deamidating proteins using an enzyme, which directly acts upon the amide groups without causing severing of peptide bond and cross-linking of that protein with another protein or a peptide, and which appears to be a unique property of the enzyme with SEQ ID NO:6. However, claims 21, 24-26, 29-30, 33, 34, 37 are so broad as to encompass a method of deamidating proteins using any such deamidase from any source including mutants, variants and recombinants and applicants have not taught as to how one of skill in the art would be able make and use such an enzyme. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of sources broadly encompassed by the claims. Furthermore, even if one of ordinary skill in the art contemplates on making such an enzyme by recombinant methods by mutating known deamidases, the specification does not provide enablement for such methods. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a

protein's amino acid sequence to obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one such amidase.

While enzyme isolation and characterization methods are known in the art, it is not routine in the art to screen exhaustively large number of sources to find the desired enzyme and such screening would also cause undue experimentation to one of ordinary skill in the art. Similarly, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications of known deamidases, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all sources of the enzyme and all modifications and fragments of any amidase because the specification does not establish: (A) a rational and predictable scheme for isolating the enzyme from any or all given sources; (B) a rational and predictable scheme for modifying any known amidase amino acid residue with an expectation of obtaining the desired biological function; (C) regions of the protein (any amidase) structure which may be modified; (D) the general tolerance

of deamidases to modification and extent of such tolerance; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including deamidases isolated from any source. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, identification and determination of amidase having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have traversed the above rejection arguing that the specification fully and adequately describes methods for screening microorganisms capable of producing the above enzyme and in addition also teaches that the claimed invention can be obtained from the microorganisms by utilizing the hybridization and PCR methods. Applicants argue that with all the information those skilled in the art can conduct the isolation, purify and characterize the enzyme without undue experimentation. Applicants also draw the attention f the Examiner to the new claims drawn to the enzyme derived from *Chryseobacterium* and submit that such claims are also fully supported by the specification. Examiner respectfully disagrees with such an argument and does not believe that it is persuasive to overcome the above rejection. Examiner also directs the applicants attention to the interpretation of the phrase "derived from...." by the Examiner (see above). Examiner submits

that above claims are overly broad and encompasses enzymes with similar activity from all or any sources, including all microbes, plants, animals and variants, mutants and recombinants including those man-made variants with any structure as well. For example, just one of the above group "microorganisms" is so diverse that it includes all types of bacteria known to man, all types of yeasts and fungi known to man, all types of blue green algae known to man and all types of microscopic animal cells that mostly comprise the division of protozoa. Thus by claiming the enzyme from all sources, applicants are claiming an enormously large group of source for which a representative number itself would necessarily be large. Next, applicants have shown that the above characteristic feature (i.e., the presence of the enzyme) only in one microorganism. Applicants have not shown that this above enzyme is produced by a large number of microorganisms or other biological sources. While microbial isolation and identification techniques are known, it is not routine in the art to screen for multiple strains, as encompassed by the instant claims, and a reasonable expectation of success in obtaining the desired activity/utility are limited and the results of such identifications are unpredictable.

Examiner has concluded that the specification does not support the broad scope of the claims which encompass all or any source of the enzyme with the above characteristics based on the following analysis: (A, Breadth of the claim) Applicants have not shown that the assay they provide to identify the microorganism is suitable to test any source or microorganism, i.e., any bacteria, any yeast any fungi, any cyanobacteria or any protozoal cell or any plant or any animal cell. The assay they have provided is mainly for the bacterial cells. While applicants may argue that the assay they have provided is enough to identify the enzyme from any source, Examiner disagrees with such an argument. This is because, just among bacteria there are different sub

groups. For example there are aerobes and anaerobes. Anaerobic bacteria do not grow in the presence of air (or oxygen) and applicants have not shown as to how one skilled in the art would use their assay in the case of anaerobes. Similarly, Examiner can list a large number of groups of microorganisms plants and animals which are highly diverse and no single method or assay would apply to all of them. However, providing such a list is beyond the scope of this rejection and impractical. B. (Nature of the invention) Applicants have not shown that the enzyme is universal in all sources. Applicants have argued that the assay they have provided is quite enough to identify any source. Examiner respectfully disagrees. This is because of the nature of invention. For example, it is well known in the art of the microbiology that microbes invariably have alternate pathways for making or breaking a compound. While applicants are claiming that they have provided an assay (which is based on assaying for the presence of an amidase) it is highly likely that alternate pathways may be present in nature, and because of this the assay provided by the applicants may not work on all microorganisms. C. (State of the prior art) The prior art is not rich in the above type of inventions i.e., the subject matter of the above invention is practiced by a small group of inventors and there is no information regarding the capability of all the different types of bacteria or yeasts or fungi or the cyanobacteria etc. to produce the above enzyme. Applicants have also not shown the above ability of any other type of bacteria or fungi or yeast or a cyanobacteria or a microscopic protozoan. Therefore, there are no examples of the above invention in the prior art. D. (level of ordinary skill) The specification does not provide a universal method that can be used by any one skilled in the art. This is because, while the specification simply provides the assay method that can be performed by one skilled in the art familiar with *Chryseobacterium*, applicants have not provided enough guidance as to how one

interested in isolating a thermophilic bacteria or psychrophilic bacteria or anaerobic bacteria or a fungi, a yeast or a microscopic protozoan would use the assay method for isolating the claimed microorganisms. The above groups of microorganisms have special culture requirements and applicants have not provided enough guidance such that their method can be used for testing any of the above microorganism. E (level of predictability in the art/ amount of direction provided by the inventor/existence of working examples) While predictability is quite straight forward in mechanical and electrical arts, it is highly unpredictable in bioscience arts. This aspect has been well understood in all court decisions. Therefore, while applicants claim that the assay they provide would be able to identify any microorganism, because of the complexity of the microbial cells, an assay that is applicable for one type of microorganism may be completely useless for another group. For example it has been acknowledged in *In re Fisher*, 427 F.2d 833, 839,166 USPQ 18, that in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required and in applications directed to inventions in art where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims, *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). F.(quantity of experimentation needed to make the invention) The specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. This is because applicants have not provided a method or methods that can be used to identify any microorganism.

Thus, applicants have <u>not</u> provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the enzyme from all or any source. The scope of the claims must

bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, identification of a microorganism having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 21, 24-26, 29-30, 33, 34, 37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 21, 24-26, 29-30, 33, 34, 37 are directed to a method of deamidating proteins using enzymes from any source. Claims 21, 24-26, 29-30, 33, 34, 37 are rejected under this section of 35 USC 112 because the claims are directed to a method which uses a genus of polypeptides (derived from any source including recombinantly modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution) that have not been disclosed in the specification. No description has been provided of all the polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:6 has been provided by applicants which would indicate that they had possession of the claimed genus of polypeptides. The specification does not contain any disclosure of the structure of all the polypeptides including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the

attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to previous Office action, applicants have traversed the above rejection arguing that the Examiner is too restrictive and that they have shown in Examples that many strains of *Chryseobacterium*, other than *C.gleum* JCM 2410 produce the above enzyme. Applicants also argue that the inventive enzyme can be distinguished from known transglutaminases and that Examiner has not given any reason to doubt applicants' disclosure as supported by the examples. First of all, Examiner respectfully disagrees with the applicants comments that he is too restrictive. Above claims simply fail the test of written description requirement. Applicants' argument that they have provided many strains of the above bacterium producing the above enzyme is not persuasive to overcome the above rejection, because, claims encompass enzymes not just from strains of *Chryseobacterium* but all or any source for which applicants have not provided the structure. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus,**

one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genus of enzymes includes species which are widely variant in structure. As such, neither the description of the structure and function of SEQ ID NOS:6 nor the disclosure solely functional features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus. Therefore Examiner maintains the above rejection.

Allowable Subject Matter

Claims 27, 28, 31, 32, 35, 36, are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1600

Manjunath N. Rao
April 28, 2003